REMARKS

I. Status of the Claims

Claims 1, 3-6, 9-24, and 26 are pending. Claims 6 and 10-24 are withdrawn. Claims 2, 7-8, and 25 are canceled without prejudice or disclaimer. Applicants reserve the right to file one or more continuing applications to any canceled subject matter.

Applicants thank Examiner Ton for extending to the undersigned the courtesy of taking their June 13, 2006, telephone enquiry. Pursuant to that discussion, Applicants respectfully request entry of the amendment presented herein so as to place the claims in suitable condition for allowance. Applicants do not in any way acquiesce with the Office's point of view regarding enablement, but simply seek to expedite examination by incorporating a phenotypic embodiment into claim 1. That amendment addresses the Office's allegation that the invention is "not enabled because the claims fail to recite an appropriate phenotype for the instantly claimed mice." Office action at page 7, lines 21-23.

Hence to advance prosecution, Applicants have amended claim 1 to incorporate the phenotypic subject matter of previously presented claim 25 (of record). See page 2 of the office action ("claims 1, 3-5, 9 and 25 are under current examination"). Claim 25 was drawn to an embodiment that required expression of the CYP3A4 family gene to be inducible by "a compound." Applicants actually discussed this embodiment in an earlier, formal telephone interview with Examiner Ton and her supervisor Examiner Woitach on May 3, 2005. See the Interview Summary dated May 12, 2005, regarding the claim set that Applicants faxed to the Office on May 2nd, which included Applicants' proposed version of claim 25. Applicants subsequently amended the claims on May 25, 2005, to make that desired phenotypic "compound" embodiment of record.

Accordingly, that part of Applicants' invention, namely the requirement that expression of a CYP3A4 gene can be induced by a generic compound, is not new. By incorporating that phenotypic "compound" embodiment into claim 1, Applicants simply make clear that claim 1 (as opposed to claim 25) "recite[s] an appropriate phenotype for the instantly claimed mice" as required by the Office (office action at page 7, lines 21-23). Applicants assert that incorporation of the subject matter of claim 25 into claim 1, therefore,

does not impose any search burden on the Office. The amendment does not introduce new matter and does not necessitate a new search.

In order to further accelerate this case toward an allowance, Applicants also take this opportunity to add claim 26 to qualify the generic compound of claim 1 as "rifampicin." The Office acknowledges that "the specification provides a working example that shows that the mouse's cells are inducible by rifampicin" (office action at page 7, lines 25-26).

Applicants assert that these after-final amendments do not introduce new matter and that the Office does not need to perform any new searches. Applicants further assert that, in accordance with MPEP Section 714.12 and 37 CFR 1.116, their amendments "place the application either in condition for allowance or in better form for appeal" and therefore "may be entered."

II. An enablement rejection based on the grounds that an alleged critical limitation is missing from a claim should be made only when the language of the specification makes it clear that the limitation is critical for the invention to function as intended

Claims 1, 3-5, 9 and 25 are rejected under 35 U.S.C. § 112, first paragraph because those claims are allegedly not enabled. The Examiner maintains that the chromosomal fragment E22 is "essential to the claimed *method*" (emphasis added; office action at page 3). Applicants do not claim any method in the present case. The examined claims are directed to a mouse and a cell. Accordingly, Applicants do not address this misnomer.

More on point, however, is the Examiner's contention that the claimed mouse is "dependent upon the fragment used [and that] the E22 fragment is considered essential . . . [hence] the fragment *itself* must be disclosed in a repeatable process in order to fulfill the requirements of 'how to make' under 112, 1st paragraph." Office action at page 5.

According to Section 2164.08(c) of the Manual of Patent Examination and Procedure,

> A feature which is **taught as critical** in a specification and is not recited in the claims should result in a rejection of such claim under the enablement provision section of 35 U.S.C. 112. See *In re Mayhew*, 527 F.2d 1229, 1233, 188 USPQ 356, 358 (CCPA 1976). In determining whether an

> unclaimed feature is critical, the entire disclosure must be considered. **Features which are merely preferred are not to be considered critical**. *In re Goffe*, 542 F.2d 564, 567, 191 USPQ 429, 431 (CCPA 1976). (Emphasis added).

Furthermore, Section 2164.08(c) provides that:

> Limiting an applicant to the preferred materials in the absence of limiting prior art would not serve the constitutional purpose of promoting the progress in the useful arts. Therefore, an enablement rejection based on the grounds that a disclosed critical limitation is missing from a claim **should be made only when the language of the specification makes it clear that the limitation is critical for the invention to function as intended**. Broad language in the disclosure, including the abstract, omitting an allegedly critical feature, tends to rebut the argument of criticality. (Emphasis added).

Similarly, Section 2172.01 states that:

> A claim which omits matter **disclosed to be essential** to the invention as described in the specification or in other statements of record may be rejected under 35 U.S.C. 112, first paragraph, as not enabling. (Emphasis added).

Indeed, the *Goffe* court held that a patent claim must adequately protect applicant's claimed invention otherwise a competitor need only follow the applicant's specification to find a substitute to the non-essential but recited claim element.

The chromosomal fragment, E22, is not essential for making the claimed invention operative. As Applicants have stressed throughout prosecution and as they related in their patent application specification, *any* chromosomal fragment that possesses the recited cytochrome genes can be incorporated into the claimed mouse.

A mouse that comprises the Ohshima chromosomal fragment instead of the E22 fragment is not inoperative simply because its chromosomal termini are different. The important patentable issue is that both the Ohshima fragment and the E22 fragment comprise the same recited cytochrome genes, which are subsequently expressed in the mouse cell when exposed to a compound, such as rifampicin.

The specification fully supports and enables the mouse of claim 1, which comprises a CYP3A4-containing fragment that has been produced by a repeatable method, and which exhibits a recited phenotype that is directly attributed to the inducible expression of a CYP3A4 gene contained on that fragment. Applicants point the Office to pages 6-10 of their paper dated December 19, 2005, where they previously stressed the predictability of the disclosed methods and the specification's enabling disclosure in this regard.

For these reasons, the specification more than sufficiently enables the skilled person therefore under the requirements of 35 U.S.C. § 112, first paragraph, to repeatedly and successfully produce a human chromosome fragment other than E22 that contains CYP3A4 genes, and to produce a mouse containing that fragment.

Applicants assert that these remarks concerning the non-essential nature of the "E22" fragment, and their present claim amendments, place this application in condition for allowance. Applicants respectfully request withdrawal therefore of the rejection of claims 1, 3-5, 9 and 25 under 35 U.S.C. § 112, first paragraph. Applicants invite Examiner Ton to contact the undersigned if she feels that a telephone discussion would further help expedite an allowance.

Respectfully submitted,

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